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Amendments to the Claims:

Please amend claims 1, 34, and 71 as provided below.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.   (Currently Amended) A computer readable medium or media having stored thereon computer-implemented instructions causing a processor to perform the steps of:

(a)   providing a data structure comprising a stoichiometric matrix relating a plurality of reactants to a plurality of reactions of a biochemical reaction network of an organism, wherein each of said reactions comprises a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product, and wherein at least one of said reactions is a regulated reaction;

(b)   providing a constraint set for said plurality of reactions of said organism, wherein said constraint set comprises a variable constraint for said regulated reaction;

(c)   solving a mathematical optimization problem using said stoichiometric matrix by determining at least one flux distribution that minimizes or maximizes an objective function when said constraint set is applied to said data structure, wherein said at least one flux distribution determines a systemic property predictive of said biochemical reaction network of said organism, and wherein said systemic property is dependent upon the flux through said regulated reaction; and

(d)   providing information resulting from steps (a) through (c) to a user.

2.   (Original) The computer readable medium or media of claim 1, wherein said variable constraint is dependent upon the outcome of at least one reaction in said data structure.

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3.   (Original) The computer readable medium or media of claim 1, wherein said variable constraint is dependent upon the outcome of a regulatory event.

4.   (Original) The computer readable medium or media of claim 1, wherein said variable constraint is dependent upon time.

5.   (Original) The computer readable medium or media of claim 1, wherein said variable constraint is dependent upon the presence of a biochemical reaction network participant.

6.   (Original) The computer readable medium or media of claim 5, wherein said participant is selected from the group consisting of a substrate, product, reaction, protein, macromolecule, enzyme and gene.

7.   (Original) The computer readable medium or media of claim 1, wherein said biochemical reaction network comprises metabolic reactions.

8.   (Original) The computer readable medium or media of claim 1, further comprising a regulatory data structure, wherein said variable constraint is dependent upon an outcome of a regulatory event represented by said regulatory data structure.

9.   (Original) The computer readable medium or media of claim 8, wherein said regulatory data structure represents a regulatory event selected from the group consisting of transcription of a gene, translation of an RNA, post-translational modification of a protein, inhibition of a protein, activation of a protein, assembly of a protein, change in pH, change in redox potential, change in temperature, passage of time, and degradation of a protein.

10.   (Original) The computer readable medium or media of claim 8, wherein said regulatory event is due to a signal transduction pathway.

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11.   (Original) The computer readable medium or media of claim 8, wherein said biochemical reaction network and said regulatory data structure represent reactions or events that occur in a single cell.

12.   (Original) The computer readable medium or media of claim 8, wherein said biochemical reaction network represents reactions that occur in a first cell in a population of cells and said regulatory data structure represents events that occur in a second cell in said population.

13.   (Original) The computer readable medium or media of claim 12, wherein said population of cells comprises cells of a multicellular organism.

14.   (Original) The computer readable medium or media of claim 1, further comprising a constraint function that correlates an outcome of a regulatory event with said variable constraint.

15.   (Original) The computer readable medium or media of claim 14, wherein said constraint function is binary.

16.   (Original) The computer readable medium or media of claim 14, wherein said regulatory event is represented by Boolean logic.

17.   (Canceled)

18.   (Previously Presented) The computer readable medium or media of claim 1, further comprising a range of said feasible flux distributions.

19.   (Previously Presented) The computer readable medium or media of claim 1, wherein said commands comprise an optimization problem.

20.   (Original) The computer readable medium or media of claim 19, wherein said optimization problem comprises a linear optimization problem or a nonlinear optimization problem.

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21.   (Previously Presented) The computer readable medium or media of claim 1, further comprising a user interface capable of sending at least one command for modifying said data structure, said constraint set or said commands for applying said constraint set to said data representation, or a combination thereof.

22.   (Original) The computer readable medium or media of claim 21, wherein said user interface further comprises links which a user may select to access additional information relating to said plurality of reactions.

23.   (Original) The computer readable medium or media of claim 1, wherein said data structure comprises a set of linear algebraic equations.

24.   (Original) The computer readable medium or media of claim 1, wherein said data structure comprises a matrix.

25.   (Original) The computer readable medium or media of claim 1, further comprising commands for representing said at least one flux distribution as a flux distribution map.

26.   (Original) The computer readable medium or media of claim 1, wherein at least one reactant in said plurality of reactants or at least one reaction in said plurality of reactions is annotated.

27.   (Original) The computer readable medium or media of claim 26, wherein said annotation comprises assignment of said at least one reactant to a compartment.

28.   (Original) The computer readable medium or media of claim 27, wherein a first substrate or product in said plurality of reactions is assigned to a first compartment and a second substrate or product in said plurality of reactions is assigned to a second compartment.

29.   (Original) The computer readable medium or media of claim 26, wherein said annotation comprises assignment to an open reading frame or protein.

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30. (Previously Presented) The computer readable medium or media of claim 26, wherein said annotation comprises a confidence limit for occurrence of a reaction.

31. (Original) The computer readable medium or media of claim 1, further comprising a gene database relating one or more reactions in said data structure with one or more genes or proteins in particular organism.

32. (Original) The computer readable medium or media of claim 1, wherein said biochemical reaction network comprises reactions that are selected from the group consisting of glycolysis, the TCA cycle, the pentose phosphate pathway, respiration, biosynthesis of an amino acid, degradation of an amino acid, biosynthesis of a purine, biosynthesis of a pyrimidine, biosynthesis of a lipid, metabolism of a fatty acid, biosynthesis of a cofactor, metabolism of a cell wall component, transport of a metabolite and metabolism of carbon, nitrogen, sulfur, phosphate, hydrogen or oxygen.

33. (Original) The computer readable medium or media of claim 1, wherein a plurality of said reactions are regulated reactions and said constraints for said regulated reactions comprise variable constraints.

34. (Currently Amended) A method for determining a systemic property of a biochemical reaction network of an organism, comprising:

    (a) providing a data structure comprising a stoichiometric matrix relating a plurality of reactants to a plurality of reactions of a biochemical reaction network of an organism, wherein each of said reactions comprises a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product, and wherein at least one of said reactions is a regulated reaction;

    (b) providing a constraint set for said plurality of reactions of said organism, wherein said constraint set comprises a variable constraint for said regulated reaction;

    (c) providing a condition-dependent value to said variable constraint;

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(d)   providing an objective function;

(e)   <u>solving a mathematical optimization problem using said stoichiometric matrix by</u> determining on a computer at least one flux distribution that minimizes or maximizes said objective function when said constraint set is applied to said data structure,

wherein said at least one flux distribution is determinative of a systemic property <u>predictive</u> of said biochemical reaction network <u>of said organism;</u> and

(f)   providing said systemic property of said biochemical reaction network to a user.

35.   (Previously Presented) The method of claim 34, wherein said condition-dependent value provided to said variable constraint comprises a value conditioned on the outcome of at least one reaction in said data structure.

36.   (Previously Presented) The method of claim 34, wherein said condition-dependent value provided to said variable constraint comprises a value conditioned on the outcome of a regulatory event.

37.   (Previously Presented) The method of claim 34, wherein said condition-dependent value provided to said variable constraint comprises a value conditioned on time.

38.   (Previously Presented) The method of claim 34, wherein said condition-dependent value provided to said variable constraint comprises a value conditioned on the presence of a biochemical reaction network participant.

39.   (Original) The method of claim 38, wherein said participant is selected from the group consisting of a substrate, product, reaction, enzyme, protein, macromolecule and gene.

40.   (Original) The method of claim 34, wherein said biochemical reaction network comprises metabolic reactions.

41.   (Previously Presented) The method of claim 34, wherein said data structure further comprises a regulatory data structure, wherein said value provided to said variable

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constraint is changed due to an outcome of a regulatory event represented by said regulatory data structure.

42.   (Original) The method of claim 41, wherein said regulatory event is selected from the group consisting of transcription of a gene, translation of an RNA, post-translational modification of a protein, inhibition of a protein, activation of a protein, assembly of a protein, change in pH, change in redox potential, change in temperature, passage of time, and degradation of a protein.

43.   (Original) The method of claim 41, wherein said regulatory event is due to a signal transduction pathway.

44.   (Original) The method of claim 41, wherein said biochemical reaction network and said regulatory data structure represent reactions or events that occur in a single cell.

45.   (Original) The method of claim 41, wherein said regulatory event comprises a regulatory reaction.

46.   (Original) The method of claim 41, wherein said biochemical reaction network represents reactions that occur in a first cell in a population of cells and said regulatory data structure represents events that occur in a second cell in said population.

47.   (Original) The method of claim 46, wherein said population of cells comprises cells of a multicellular organism.

48.   (Original) The method of claim 41, further comprising a constraint function that correlates an outcome of a regulatory event with said variable constraint.

49.   (Original) The method of claim 48, wherein said constraint function is binary.

50.   (Original) The method of claim 48, wherein said regulatory event is represented by Boolean logic.

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51.   (Original) The method of claim 48, wherein said constraint function correlates a first set
       of outcomes of said regulatory data structure with a first binary value and a second set of
       outcomes of said regulatory data structure with a second binary value.

52.   (Original) The method of claim 48, wherein said constraint function correlates a set of
       outcomes of said regulatory data structure with a single integer value.

53.   (Original) The method of claim 34, wherein said flux distribution is determined by
       optimization.

54.   (Original) The method of claim 53, wherein said optimization comprises linear
       optimization or non linear optimization.

55.   (Original) The method of claim 34, further comprising a step of modifying said data
       structure or said constraint set, or both.

56.   (Original) The method of claim 34, wherein said data structure comprises a set of linear
       algebraic equations.

57.   (Original) The method of claim 34, wherein said data structure comprises a matrix.

58.   (Original) The method of claim 34, further comprising a step of producing a flux
       distribution map.

59.   (Original) The method of claim 34, wherein said biochemical reaction network
       comprises reactions that are selected from the group consisting of glycolysis, the TCA
       cycle, pentose phosphate pathway, respiration, biosynthesis of an amino acid, degradation
       of an amino acid, biosynthesis of a purine, biosynthesis of a pyrimidine, biosynthesis of a
       lipid, metabolism of a fatty acid, biosynthesis of a cofactor, metabolism of a cell wall
       component, transport of a metabolite and metabolism of a carbon source, nitrogen source,
       oxygen source, phosphate source, hydrogen source or sulfur source.

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60. (Original) The method of claim 34, wherein said systemic property is selected from the group consisting of growth, energy production, redox equivalent production, biomass production, production of biomass precursors, production of a protein, production of an amino acid, production of a purine, production of a pyrimidine, production of a lipid, production of a fatty acid, production of a cofactor, production of a cell wall component, transport of a metabolite, development, intercellular signaling, and consumption of carbon nitrogen, sulfur, phosphate, hydrogen or oxygen.

61. (Original) The method of claim 34, wherein said systemic property is selected from the group consisting of degradation of a protein, degradation of an amino acid, degradation of a purine, degradation of a pyrimidine, degradation of a lipid, degradation of a fatty acid, degradation of a cofactor and degradation of a cell wall component.

62. (Original) The method of claim 34, wherein said variable constraint comprises a condition-dependent constraint value and a constraint function, wherein said variable constraint is modified by said constraint function acting upon said condition-dependent constraint value.

63. (Original) The method of claim 62, wherein said constraint function is binary.

64. (Original) The method of claim 34, further comprising providing a gene database relating one or more reactions in said data structure with one or more open reading frames or proteins in a particular organism.

65. (Original) The method of claim 64, further comprising identifying an open reading frame that encodes a protein that performs a reaction in said plurality of reactions.

66. (Withdrawn) The method of claim 64, further comprising identifying a protein that performs a reaction in said plurality of reactions.

67. (Withdrawn) A method for determining a phenotype of a mutant of an organism, comprising:

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(i)   identifying a reaction that is not naturally present in a particular organism, and

(ii)   determining a systemic property of a biochemical reaction network according to the method of claim 34, wherein said data structure relates a plurality of reactants for said organism to a plurality of reactions of a biochemical reaction network of said organism and further comprises said reaction that is not naturally present in said organism.

68.   (Withdrawn)   A method for determining a phenotype of a mutant of an organism, comprising:

(i)   identifying a reaction that is related to an open reading frame or protein in said gene database, and

(ii)   determining a systemic property of a biochemical reaction network according to the method of claim 34, wherein said reaction that is related to said open reading frame or protein is not present in said data structure or is constrained to have no flux.

69.   (Withdrawn)   A method for determining the effect of a drug on the activity of one or more reactions in a biochemical reaction network, comprising:

(i)   identifying a reaction that is related to an open reading frame or protein in said gene database;

(ii)   identifying a candidate drug that alters expression of said open reading frame or activity of said protein, and

(iii) determining a systemic property of a biochemical reaction network according to the method of claim 34, wherein said reaction that is related to said open reading frame or protein is not present in said data structure, is constrained to have a reduced flux, or is constrained to have no flux.

70.   (Original)   The method of claim 34, wherein a plurality of said reactions are regulated reactions and said constraints for said regulated reactions comprise variable boundary values.

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71.   (Currently Amended) A method for determining a systemic property of a biochemical reaction network at a first and second time, comprising:

    (a)   providing a data structure comprising a stoichiometric matrix relating a plurality of reactants to a plurality of reactions of a biochemical reaction network of an organism,

wherein each of said reactions comprises a reactant identified as a substrate of the reaction, a reactant identified as a product of the reaction and a stoichiometric coefficient relating said substrate and said product, and wherein at least one of said reactions is a regulated reaction;

    (b)   providing a constraint set for said plurality of reactions of said organism, wherein said constraint set comprises a variable constraint for said regulated reaction;

    (c)   providing a condition-dependent value to said variable constraint;

    (d)   providing an objective function;

    (e)   solving a mathematical optimization problem using said stoichiometric matrix by determining on a computer at least one flux distribution at a first time that minimizes or maximizes said objective function when said constraint set is applied to said data structure, thereby determining a systemic property predictive of said biochemical reaction network of said organism at said first time;

    (f)   modifying said value provided to said variable constraint;

    (g)   repeating step (e) wherein said at least one flux distribution is determined at a second time, thereby determining a systemic property predictive of said biochemical reaction network of said organism at a second time, and

    (h)   providing said systemic property of said biochemical reaction network to a user at said first, second or first and second time.

72.   (Original) The method of claim 71, wherein said value is modified based on said flux distribution at said first time.

73.   (Original) The method of claim 71, wherein said value is modified based on a change in an environmental condition.

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74.   (Original) The method of claim 71, further comprising repeating steps (e) through (g) for a specified number of timepoints.